

Serial No. 10/800,992  
Docket No: D-2804CON2

**REMARKS**

Applicants are in receipt of the Office Action mailed June 2, 2008. Following a careful review of this Office Action, Applicants have the following comments.

Applicants appreciate the Examiner's indication that the arguments filed February 12, 2008 were persuasive regarding previous rejections of record.

Rejection pursuant to 35 USC §103(a)

The Examiner has rejected claims 31-51 over the combination of Loftsson et al., U.S. Patent. No. 5472,954, Lipari U.S. Patent No. 4,383,992, Remington's Pharmaceutical Sciences, and Dziabo et al., 5,424,078. Following careful consideration, Applicants respectfully traverse this rejection.

In summary, the Office Action alleges that Loftsson discloses an ophthalmic composition comprising a cyclodextrin and a steroid. However, the Loftsson reference discusses a very large number of compounds (drugs, food additives, cosmetic additives and agrochemicals; see e.g., column 4, lines 1 and 2) which, Loftsson claims, may be formulated with a very large number of cyclodextrin derivatives and a very large number of selected polymers to enhance their solubility or decrease their water lability. A list of various cyclodextrins is disclosed in column 6; a large list of polymers is mentioned e.g., in column 7; a very large list of compounds to be complexed with the cyclodextrin and polymer is listed in columns 7-13. As acknowledged by the Examiner, the compound

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prednisolone acetate is not mentioned anywhere in this reference. Neither does Loftsson disclose chlorite or sorbate preservatives.

Lipari discusses compositions comprising prednisolone acetate and  $\beta$ -cyclodextrin, but does not disclose a preservative.

Dziabo et al discusses ophthalmic compositions preserved using chlorite.

Remington's discusses that prednisolone and prednisolone acetate are slightly soluble in water.

The Office Action argues that one of ordinary skill in the art would have been motivated to combine prednisolone acetate and a cyclodextrin, based on the combination of Loftsson, Lipari and Remington's, and that Dziabo provide motivation to preserve such a composition using a chlorite component such as chlorine dioxide. No mention is made of sorbate in Dziabo.

However none of the prior art discloses, as the present specification discloses, that a cyclodextrin-containing composition is not effectively preserved using many of the traditionally used ophthalmic preservatives. Perhaps the most commonly used ophthalmic preservatives are quaternary ammonium compounds such as, without limitation, benzalkonium, cocoalkonium, trimethylammonium and tallowalkonium halides (e.g., bromide and chloride), and Quaternium preservatives such as Quaternium-8, -14, -15, and -18. The experiments conducted and disclosed in the specification of this patent application indicate that the preservative effectiveness of benzalkonium chloride (BAK) in a liquid composition, as measured by the United States Preservative Efficacy Test (USPET), is reduced in the presence of cyclodextrins.

The attached Declaration under 37 CFR 1.132 is a declaration of the first-named inventor of the present invention, Gary Beck, in which he indicates that the Specification discloses that the fact that under the USPET the preservative efficacy of chlorite and sorbate were substantially unaffected by the presence of cyclodextrin was a completely unexpected result to him and his staff, particularly in light of the finding concerning other preservatives, such as quaternary ammonium preservatives. Mr. Beck concludes that a person of ordinary skill in the art would have been unable to predict this result based upon the prior art cited.

In the recent United States Supreme Court case *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. \_\_\_, \_\_\_ U.S.P.Q.2d\_\_\_ (2007), Justice Kennedy affirmed that *Graham v. John Deere*, 383 U.S. 1, 36 (1966) continues to set forth the proper analytical test for obviousness. Pursuant to *Graham*, in an obviousness analysis, "the scope and content of the prior art [at the priority date of the application in question] are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined." 383 U.S. at 17, 148 U.S.P.Q. at 467.

Under *Graham*, obviousness of a claimed invention may be disproved by the existence of evidence of non-obviousness. These so-called secondary considerations " may include evidence of commercial success, long-felt but unsolved needs, failure of others, and unexpected results. The evidence may be included in the specification as filed, accompany the application on filing, or be provided in a timely manner at some other

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point during the prosecution. Manual of Patent Examining Procedure (MPEP) §2141 (II). Thus, the objective evidence provided in the present specification and averred to by Mr. Beck in his Declaration, indicates that the present inventors identified a problem that was unmentioned by any prior art, and unexpectedly found a solution to that problem. Neither of these actions were obvious when the present patent application was filed.

When evaluating claims for obviousness "the prior art as a whole must be considered. The teachings are to be viewed as they would have been viewed by one of ordinary skill" when the present application was filed. *In re Hedges*, 783 F.2d 1038, 1041 (Fed. Cir. 1989). Furthermore, "[i]t is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art." *Id.* (citations omitted).

In a recent opinion, the Court of Appeal for the Federal Circuit has indicated that "the Supreme Court's analysis in *KSR* presumes that the record before the time of invention would supply some reasons for narrowing the prior art universe to a 'finite number of identified, predictable solutions (citation omitted). To the extent that an art is unpredictable, as the chemical arts often are, *KSR*'s focus on "identifiable, predictable solutions" may present a difficult hurdle because potential solutions are less likely to be genuinely predictable." *Eisai Co. Ltd. v. Dr. Reddy's Laboratories, Ltd.* \_\_ USPQ2d \_\_ (slip op. 2007-1397, -1398 at 8) (Fed. Cir. July 21, 2008).

In the present case, both the problem (loss of efficacy of preservatives (e.g. quaternary ammonium preservatives) in the presence of

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cyclodextrins) and particularly the presently claimed solution (chlorite and sorbate preservatives do not substantially lose efficacy in the presence of cyclodextrins) could not have been predicted before the experiments described in the specification were done.

For these reasons the present claims are thought to be in condition for allowance, and reconsideration and withdrawal of the present rejection is respectfully sought.

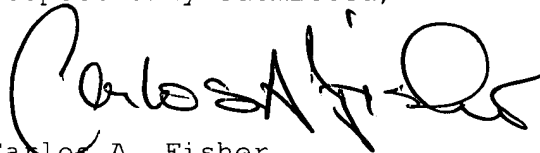
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**CONCLUSION**

For the reasons presented above the Applicants respectfully believe the claims are in condition for allowance and ask the Examiner to issue a Notice to that effect.

Applicant s hereby petition for a one-month extension of time, and enclose a check for the payment thereof. No fee is thought to be due in connection with this communication. However, if Applicants are in error in this regard, kindly use Deposit Account 21-0890 for the payment of any charge now due.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Carlos A. Fisher', with a large, stylized 'C' and 'F'.

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